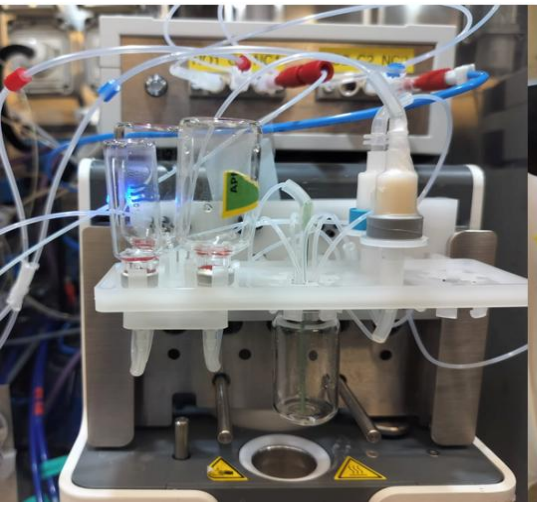
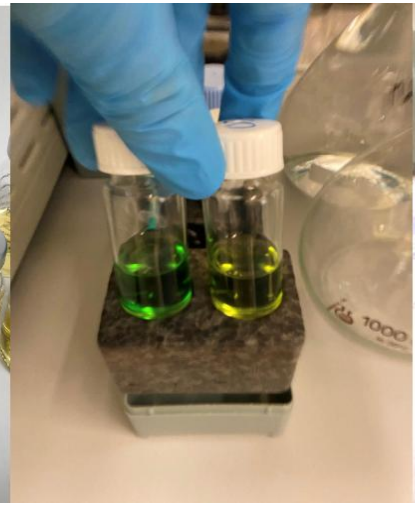
CNR - IFC Istituto
di Fisiologia Clinica





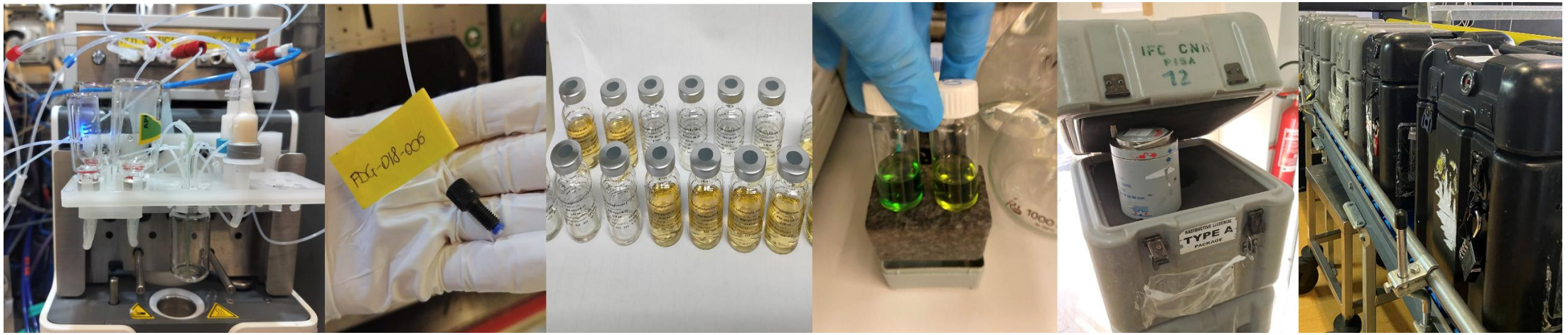



Officina Farmaceutica Istituto di Fisiologia CNR Pisa

OFFICINA FARMACEUTICA: MISSION AND AIM

The Pharmaceutical Laboratory (Officina Farmaceutica) is a small pharmaceutical industry authorized by the Italian Medicines Agency (AIFA) to produce PET radiopharmaceuticals.
It is an infrastructure of CNR in particular of the Clinical Physiology Institute (IFC).

The aim of our work is to contribute to fair treatment to all patients in the regional/national territory, especially through the distribution of innovative radiopharmaceuticals not yet available in the national territory, and to contribute to the advancement of clinical research in personalized diagnostics.



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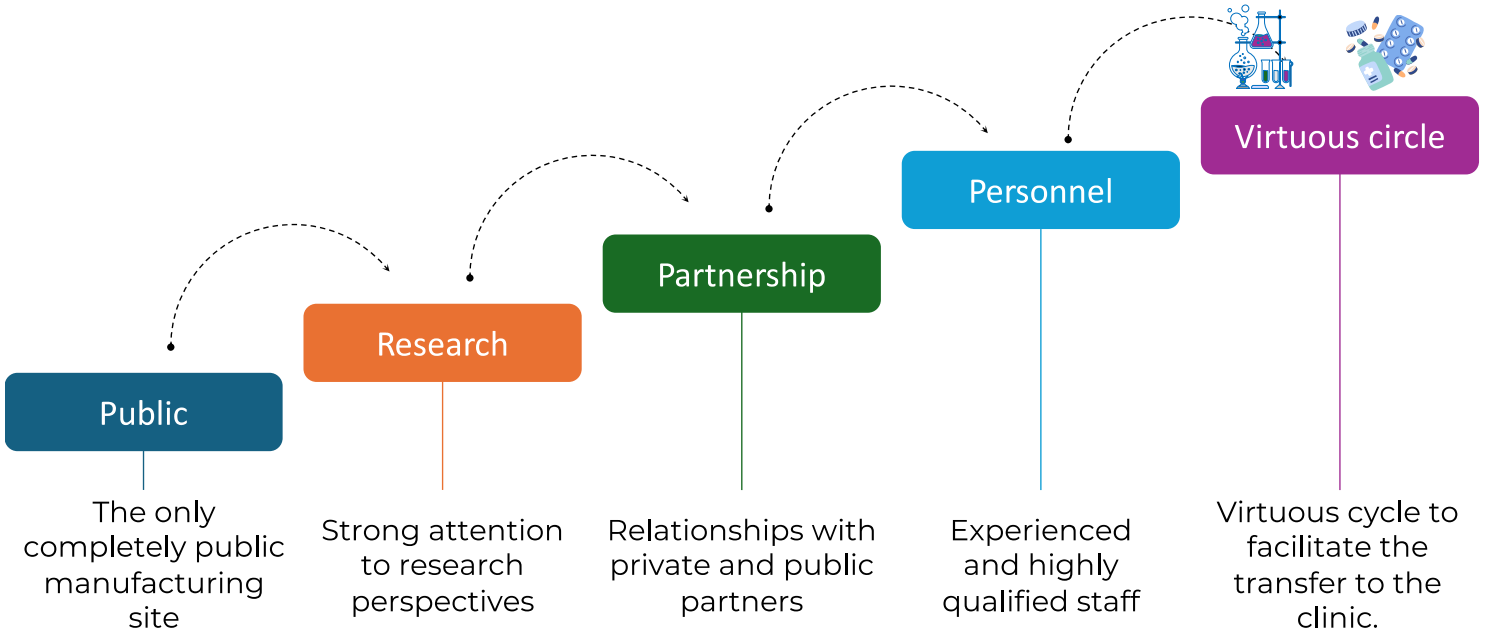
OUR PECULIARITY

This is the current situation of the radiopharmaceuticals manufacturing in Italy



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OUR AUTHORIZATIONS

We are the first Italian public manufacturing site authorized by AIFA to produce radiopharmaceuticals according to GMP.

We work in synergy and partnership with company CURIUM PHARMA, a world leader in the production of radiopharmaceuticals

We have two types of AIFA authorizations:

- **Large distribution**
  - ✓ FLUODEOXYGLUCOSE (18F)- 185 MBq/ml solution for injection Curium
  - ✓ Fluorocholine (18F) Italy 225 MBq/mL solution for injection Curium Italy
  - ✓ PYLCLARI ([18F]-DCFPyL) 1500 MBq/mL and PYLCLARI 1000 MBq/mL solution for injection Curium
  - ✓ IASOGLIO (18F-FET) 2000 MBq/mL solution for injection Curium
- **Experimental radiopharmaceuticals**
  - ✓ All 18-F-labelled radiopharmaceuticals for clinical trials

- We are also certified according to ISO 9001:2015 for the production of radiopharmaceuticals

REGULATORY ISPECTION HISTORY

2007

First 18F-FDG Authorization

2007-2014

18F-FDG Production in partnership with GEHC

2020

18F-FDG authorization

18F-FColine authorization

2021

Cyclotron Upgrade

18F-FDG Production started

2022

18F-FColine Production started

Experimental RF authorization

2023

THE project started

18F-PYL TT

2024

18F-PYL authorization

18F-FET TT

18F-FET Authorization

18F-FAPI validation

18F-DOPA TT

2025

18F-FAPI Clinical trial

18F-FET Clinical T.

18F-DOPA Authorization

18F-Prostatep TT

18F-Prostatep Authorization

SYN 2 TT

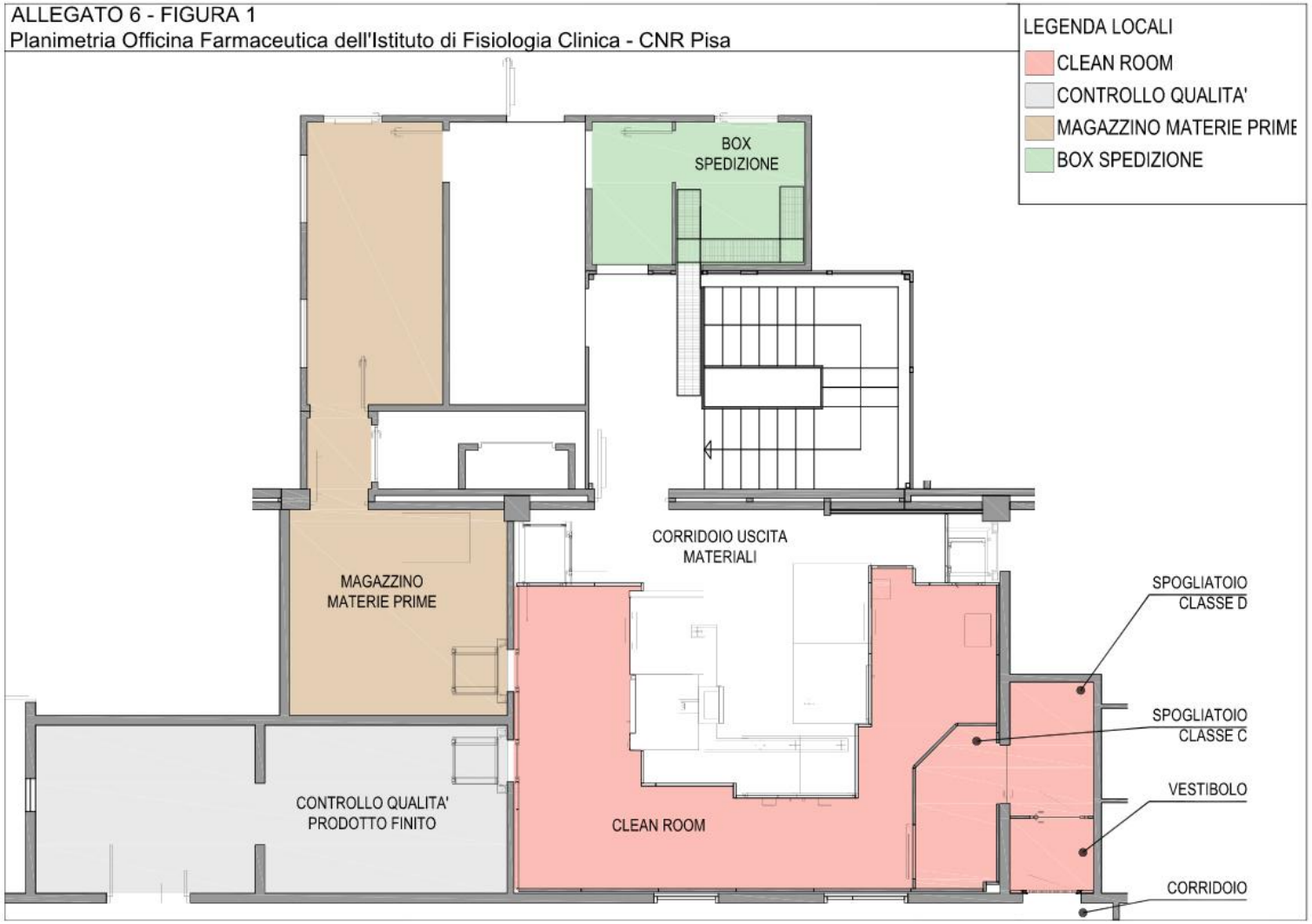
Officina 2.0
New management starts activity

18F-PYL Large distribution

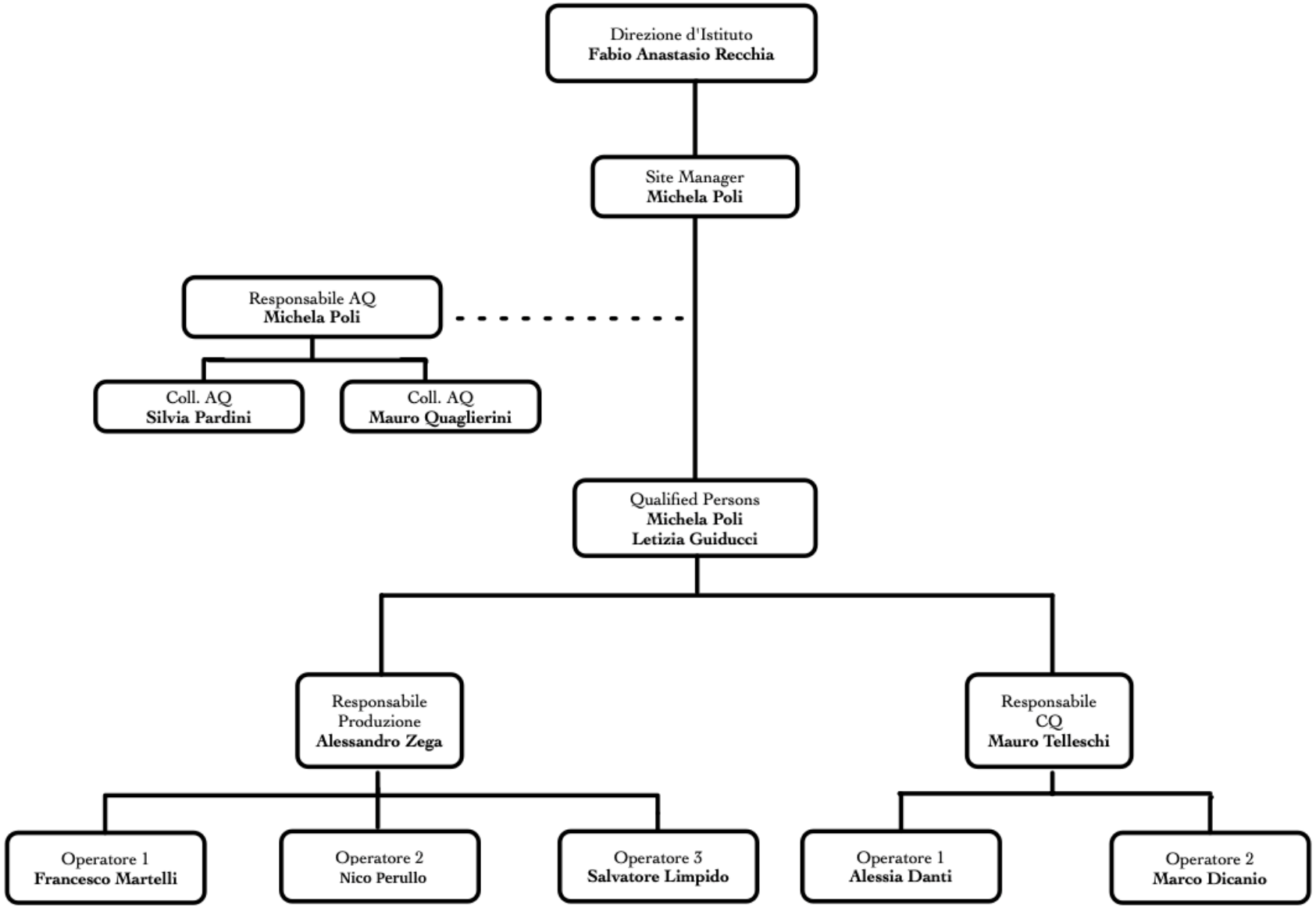
18F-Fcoline Large distribution

18F-FDG Large distribution

FACILITIES


ALLEGATO 6 - FIGURA 1
Planimetria Officina Farmaceutica dell'Istituto di Fisiologia Clinica - CNR Pisa
LEGENDA LOCALI
CLEAN ROOM
CONTROLLO QUALITA'
MAGAZZINO MATERIE PRIME
BOX SPEDIZIONE
BOX SPEDIZIONE
CORRIDOIO USCITA MATERIALI
MAGAZZINO MATERIE PRIME
CONTROLLO QUALITA' PRODOTTO FINITO
CLEAN ROOM
SPOGLIATOIO CLASSE D
SPOGLIATOIO CLASSE C
VESTIBOLO
CORRIDOIO

ORGANIZATIONAL CHART

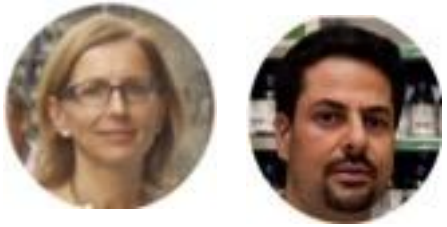


TEAM

Our team is made up of people who are part of both CNR and Curium Pharma company

Alessandro Zega (CNR,
PRD manager)
Francesco Martelli (Curium)
Salvatore Limpido (Curium)

Mauro Telleschi (CNR,
QC manager)
Alessia Danti (Curium)
Marco Dicanio (Curium)



Michela Poli (CNR
QA Manager)
Mauro Quaglierini (CNR)
Silvia Pardini (CNR)

Letizia Guiducci (CNR,
Qualified person)
Michela Poli (CNR, Site manager,
Qualified person)

Antonio Fiore
Research Fellow

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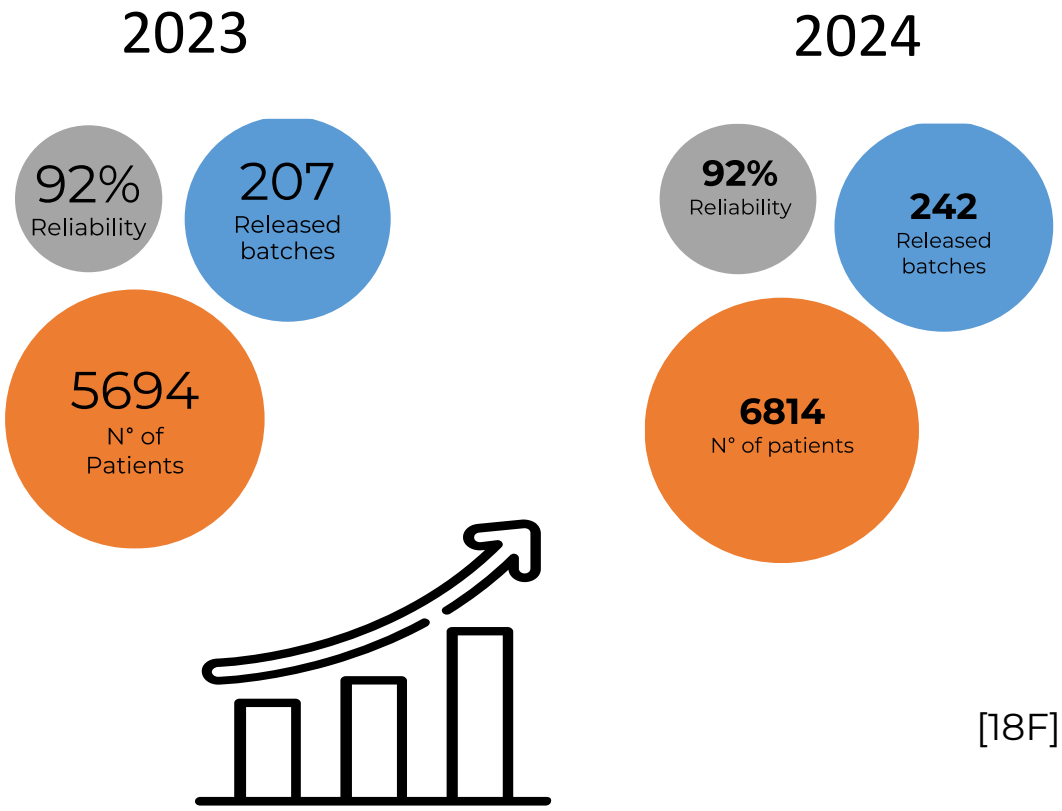
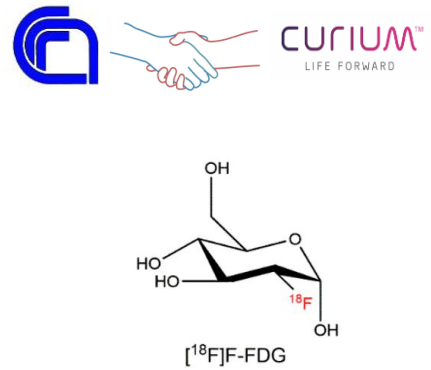
FLUODEOXYGLUCOSE (18F) 185 MBQ/ML SOLUTION FOR INJECTION

95% of all PET diagnostic studies are performed using the 2-[^{18}F]fluoro-2-deoxy- d-glucose ([^{18}F]FDG)





[18F]FDG large distribution from Pisa

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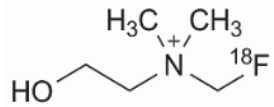
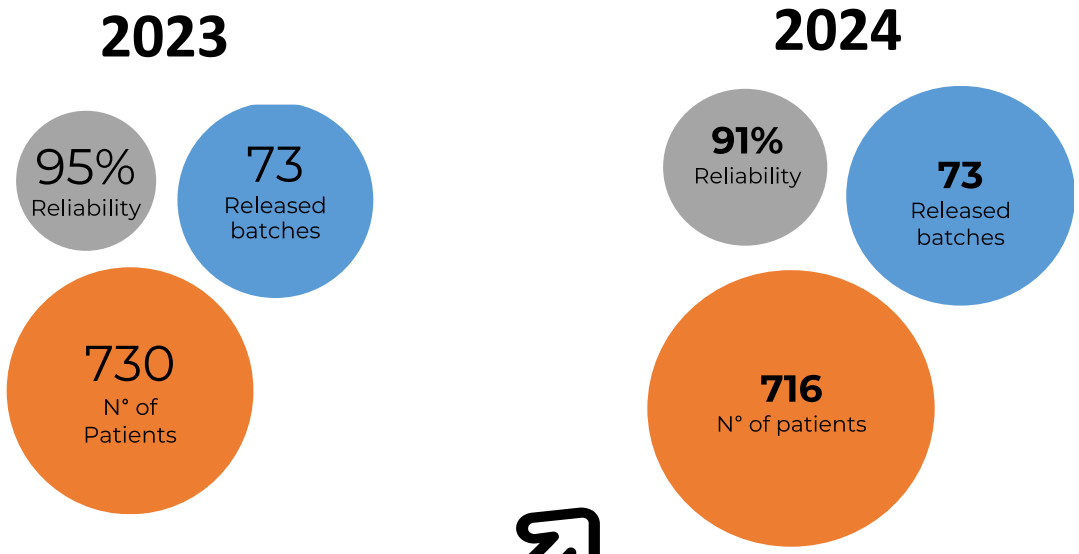
Fluorocholine (18F) 225 MBq/mL solution for injection

This radiopharmaceutical is used in the diagnosis of prostate cancer and parathyroid gland cancer. Before being produced at the Pisa site, Fluorocholine arrived in Tuscany from Austria and Udine.





Fluorocholine large distribution from Pisa

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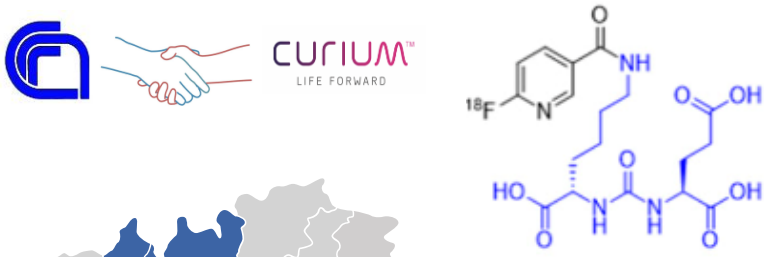
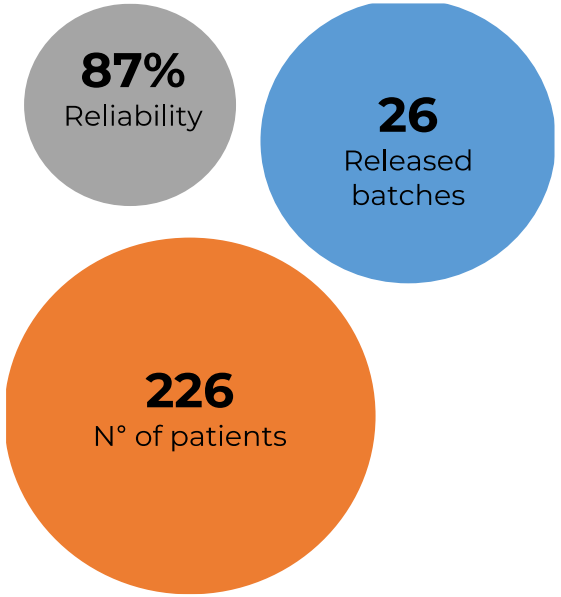
PYLCLARI® 1000 e 1500 MBq/mL solution for injection

PYLCLARI® (PSMA) is a selective inhibitor of a specific membrane antigen expressed in prostate cancer used in the primary diagnosis and in early localization of a possible recurrence of the disease

Only three radiopharmaceuticals production sites are authorised in Italy to produce PYLCLARI®: IFC-CNR, and two Curium production sites at Istituto Europeo di Oncologia in Milan and at the Policlinico Tor Vergata in Rome.





Large distribution production began in May 2024.

PYLCLARI® large distribution from Pisa

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THE - Tuscany Health Ecosystem

Spoke 1-WP8: Synthesis and production of tumor-targeted radionuclides, radiotracers and radiopharmaceuticals for clinical use

Production of radiopharmaceuticals to be used in diagnosis and follow -up of patients affected by glioblastoma in clinical trials carried-out in collaboration with the UNIPI Nuclear Medicine Department according to Good Manufacturing Practice (GMP) within the IFC-CNR Officina 2.0

- 18F-FDOPA
- 18F-FET
- 18F-FAPI74

These radiopharmaceuticals were not fully available in Tuscany and,considering the short half-life of our drugs (109 minutes), their availability in the proximity of the interested sites represents a great advantage for physicians and patients.

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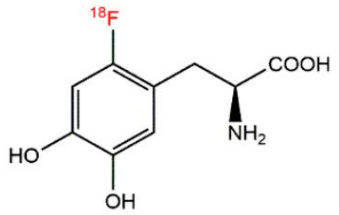
FLUORODOPA 90 MBq/mL solution for injection

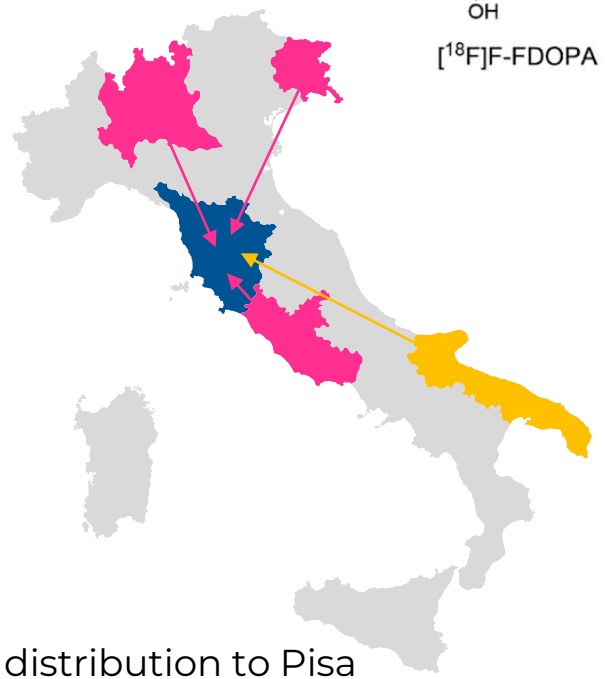
PET with Fluorodopa (18F) is indicated in neurology for the diagnosis parkinsonian syndromes.
PET with fluorodopa (18F), is also indicated in oncology for brain tumors and for the diagnosis and localization of various forms of neuroendocrine tumors.

Fluorodopa technology transfer was completed in September 2024 and AIFA application is in progress.

To date, 18F-DOPA is not available in Tuscany and it supplied by other italian regions



[18F]F-FDOPA



Florodopa large distribution to Pisa

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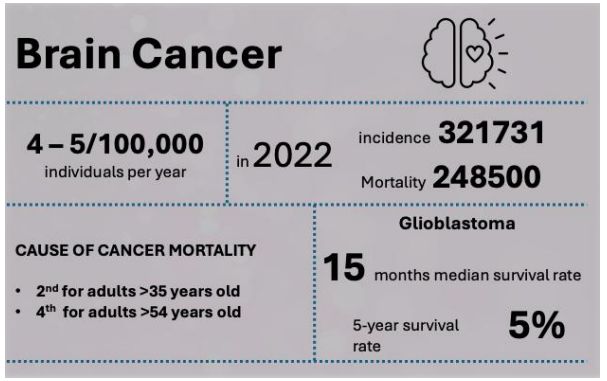
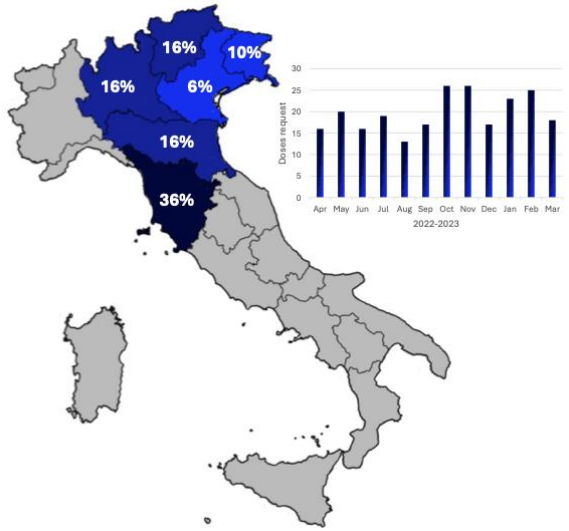
IASOGLIO® 2000 MBq/mL solution for injection

Brain tumors have a devastating impact, clinical use of 18F-FET is supported by specialized medical associations in a personalized medicine perspective. To date, 18F-FET is not available in Italy for large-scale distribution and it is imported from abroad.

IASOGLIO® technology transfer was completed in February 2024 and AIFA issued manufacturing authorization in April 2024.
Officina 2.0 was the first Italian site authorised by AIFA to produce IASOGLIO ®, the mutual recognition procedure to start large-scale distribution is underway at EMA.

The PROFETI project promoted by Curium Pharma in the context of the THE cascade calls has been awarded allowing for the extension of the TT of IASOGLIO® to the production sites of Roma Tor Vergata, Milano Istituto Europeo di Oncologia e Udine.





Technology transfer of IASOglio® drug product on Pisa PET production site
Notaro A., Poli M., Guiducci L., Bodenant V., Colombo P. 2024

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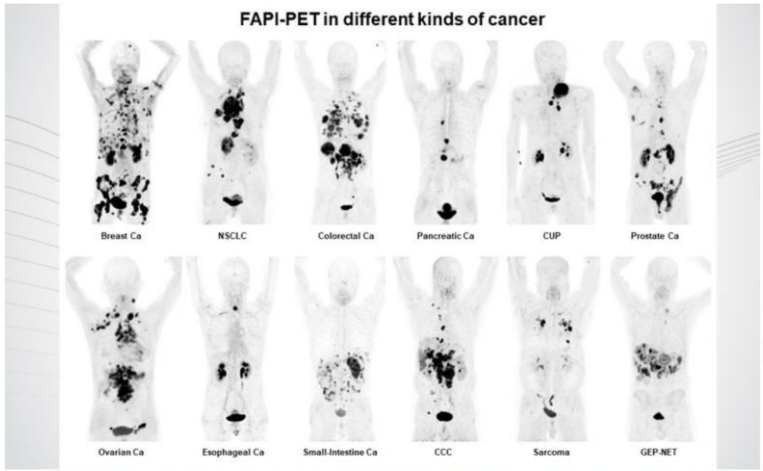
18F-FAPI74 experimental radiopharmaceuticals

[18F]FAPI-74 is a promising novel diagnostic tool for various tumors, especially for accurate staging before treatment, including characterization of tumor lesions before surgery. Moreover, 18F-labeled FAPI ligand might serve a higher demand in clinical care in the future (Watabe et al Journal of Nuclear Medicine 2023).



Source: SNMMI Image of the Year: Novel Radiotracer Detects ≥8 Cancer Types, Paving the Way for Development of New Therapies

Prospective Evaluation of [18F]FAPI PET in Intermediate Hepatocellular Carcinoma (HCC): DETECT Study.

Targeting the Tumour Microenvironment in Gliomas: A Novel FAPI-PET Approach for Predictive Imaging Biomarkers TARG Study.

In January 2025 the process validation of [18F]FAPI-74 was completed.

Batch number	Starting activity (GBq)	Activity of product (GBq)	Yield (not decay corrected)	Yield radiodecayed corrected
FAP-250108-01-PI	77.9 GBq	27.8 GBq	36%	43%
FAP-250110-01-PI	58.5 GBq	19.3 GBq	33%	39%
FAP-250113-01-PI	229.0 GBq	111.3 GBq	33%	42%

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Clinical trial SAFER 3

A Phase III Prospective, Multicenter, Open-label Study to Assess Diagnostic Efficacy of a Novel 18F-labelled Tracer, SYN2, for Positron Emission Tomography in Subjects with Suspected Coronary Artery Disease

Officina Farmaceutica will be the only producer for all 6 Italian clinical centers

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Future

Theranostics

Our expectation for the near future is to contribute to clinical trials with Lu-177-PSMA for prostate cancer or Lu-177-FAPI.

Alpha therapy with FAPI Actinium 225 in hepatic cancers in collaboration with La Sapienza University and UNIPI (FIS3)

Alpha therapy with FAPI Actinium 225 and flash radiotherapy in gliomas in collaboration with UNIPI (AIRC)

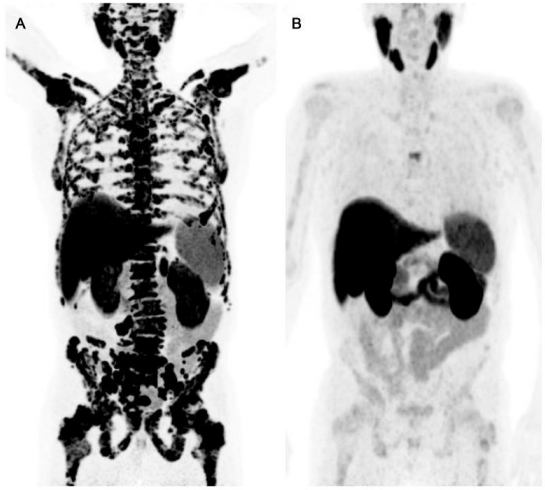

Figure 2 The 73 y/o patient with a spectacular partial response to two cycles of Lu-PSMA. 18F-PSMA-PET/CT demonstrates the tumor load before (A) and one moth after the second cycle (B). During that time PSA dropped from 121 ng/ml to 1.3 ng/ml.

Prostate Cancer Theranostics With 177Lu-PSMA
Ahmadzadehfar et al. Seminar in Nuclear Medicine 2024

Diagnostics

Diagnostica avanzata e terapie su misura per il cancro al retto in collaboration with Niguarda hospital (FESR 2021-2027)

Fluoroethoxybenzovesamicol in Alzheimer's disease in collaboration with UNIPI (FIS3)

Improvement in differential diagnosis in glioma using double tracer PET (FET and FAPI). (RF 2024)

SOCIO-ECONOMIC IMPACT

Maintenance and materials
(Curium investment)

Materials
about 220 K€ in 2024

Maintenance
about 100 K€ in 2024

Sustainability of the research infrastructure
(Radiopharmaceuticals distribution)

Cyclotron maintenace agreement
about 180 K€

Staff recruitment
(Curium investment)

5 staff units in 2024

Availability of new radiopharmaceuticals in the National area

N° of doses supplied for cancer patients near 8000 per year

Availability of new radiopharmaceuticals for clinical trials











Thank you

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michela.poli@cnr.it